

**REMARKS/ARGUMENTS**

By the present Amendment, the pending claims for examination are 1, 2, 4, 5, 7, 8, 10-16, 19, 20, 30 and 33.

The Action asserts that Claims 1-4, 7-8, 10-16, 19-21, 29-30 and 32-34 are currently pending and under examination. However, claim 5 is also still pending and should be under examination.

A clarification of the status of claim 5 is respectfully requested in the next response.

Claims 6, 9, 17, 18, 22-28 and 31 were previously canceled without prejudice or disclaimer. Additionally, claims 3, 21, 29, 32 and 34 are canceled in the present response without prejudice or disclaimer. Applicants reserve the right to file one or more CON, CIP or DIV applications.

Claims 1, 30 and 33 have been amended to recite the use of eukaryotic DNA in general and particularly Salmon sperm DNA and Calf Thymus DNA support for which is found at least in paragraph [0213] of the specification and Figures 7 and 15.

No new matter has been presented, and entry of the above revised claims is respectfully requested.

**Information Disclosure Statement (IDS)**

Enclosed herewith are forms PTO/SB/08A and PTO/SB/08B provided as a Third Supplemental IDS. Copies of documents AX, AY, AZ, BA and BB in compliance with the requirements of 37 C.F.R. §1.98(a)(2) are enclosed.

It is respectfully requested that the cited documents be expressly considered during the prosecution of this application, and the documents be made of record therein and appear among the "references cited" on any patent to issue therefrom.

Priority

Applicant thanks the Examiner for recognizing the updated status of priority application 09/104,759.

Double Patenting

Applicant thanks the Examiner for withdrawing the previous non-statutory obviousness-type double patenting rejection of claims 1-8, 10-22, 24 and 29-34.

Claim Rejections under 35 USC §103(a)

Applicant thanks the Examiner for withdrawing the previous rejection of claims 1, 17 and 18 for allegedly being unpatentable over Huang U.S. Patent No. 6,121,247 in view of Gorman U.S. Patent No. 5,830,878.

Claim Rejections under 35 USC §112, first paragraph

The rejection of claims 1-4, 7-8, 10-16, 19-21, 29-30, and 32-34 under 35 USC §112, first paragraph as allegedly not enabled such that a skilled artisan could make and/or use the invention commensurate in scope with the claims was maintained from the previous Action. The Action alleges (see page 2 of the Office Action) that while the specification is enabling for a method for eliciting a systemic, non-antigen specific immune response in a mammal, comprising administering to said mammal an amount of a composition comprising a cationic liposome delivery vehicle and an isolated bacterially-derived pCR3.1 vector without a gene insert, the specification allegedly does not reasonably provide enablement for the above when the aforementioned bacterially-derived pCR3.1 vector is replaced with a nucleic acid molecule that does not comprise bacterial sequences.

Furthermore, page four of the Office Action argues that with the exception of total salmon sperm or calf thymus DNA the specification was allegedly not found to enable

the use of any non-bacterial sequence of two or more nucleotides or any non-bacterial empty vector as a non-specific immunostimulatory molecule to treat conditions such as cancer, viral infections, and allergic inflammation.

Applicants respectfully traverse the rejection on the grounds that the currently pending claims are fully enabled by the present specification and the knowledge of the skilled practitioner. Accordingly, no *prima facie* case of non-enablement is present. However, for business considerations and without acquiescence to any position regarding patentability all of the claims of the present invention have been amended to include a cationic liposome delivery vehicle; and a eukaryotic nucleic acid molecule wherein said eukaryotic nucleic acid molecule comprises salmon sperm and/or calf thymus DNA.

Also on page 4 of the Office Action the examiner asserts that the embodiments demonstrated comprised the full chromosomal DNA content of salmon sperm or a calf thymus and as such do not qualify as a vector without a gene insert, or a fragment thereof. The claims as amended make this point moot.

The applicant successfully showed in Figures 7 and 15 that the utilization of eukaryotic salmon sperm and/or calf thymus DNA with cationic liposomes provides similar results to that shown with cationic liposomes and empty vector bacterial plasmid DNA.

As shown in Figure 7, the ability of CLDC formulated with either bacterial DNA (empty vector plasmid DNA) or eukaryotic DNA from 2 different sources (salmon sperm or calf thymus) resulted in the upregulation of splenic NK cells. Furthermore Figure 7 demonstrated that immune activation was observed when mice were injected with CLDC comprised of either eukaryotic or bacterial DNA. Injection of salmon sperm or calf thymus DNA alone did not induce CD69 upregulation.

In Figure 15 the experiment showed that the antitumor activity of CLDC (empty vector) is independent of the DNA source. In order to determine whether the antitumor

activity observed with CLDC in experiments (a) and (b) above was only a property of CLDC formulated with bacterial DNA, mice with day 3 established MCA-205 lung metastases were treated with CLDC that were formed using either plasmid (bacterial) DNA, or eukaryotic DNA (from calf thymus or salmon testis). The results in Figure 15 showed that CLDC formulated with either bacterial or eukaryotic DNA induced antitumor activity, though the bacterial DNA had slightly more potent activity.

The examiner argued many more points based on fragments and sheared sequences of DNA and the enormous number of non-bacterial nucleic acid vector sequences encompassed by applicant's claims that are moot in light of the previously described amended claim language for the salmon sperm and calf thymus DNA.

The examiner summarized the following points on pages 5 and 6 of the Office Action:

a) the enormous number of non-bacterial nucleic acid vector sequences encompassed by applicant's claims;

Argument mooted by amendment of claims as described above. Limited to calf thymus and salmon sperm DNA.

b) the lack of adequate description of any non-bacterial immunostimulatory nucleic acid sequences derived from any non-bacterial source or guidance to how such sequences can be constructed;

This argument is mooted by the above arguments discussing the Fig. 7 and Fig. 15 results as well as the claim amendments.

c) the nature of the invention and the state of the art regarding characteristics of immunostimulatory DNA sequences and the art recognized non-immunostimulatory properties of mammalian DNA;

The art of record demonstrated that it would not be expected for non-bacterial DNA to be immunostimulatory; but the present specification demonstrates that the utilization of salmon sperm and/or calf thymus DNA in conjunction with the cationic liposomes of the present invention results in an immunostimulatory and/or anti-tumor response as demonstrated in Figs. 7 and 15 of the present specification.

d) the limitations of the working examples to the use of sheared total chromosomal DNA; The claims have been amended in such a way to make this argument moot.

e) it would have required undue experimentation to identify any particular non-bacterial immunostimulatory sequences of 2 or more nucleotides or to use such sequences to produce an empty vector which does not contain bacterially derived sequence for use in the instant methods.

The amendment of the claims to salmon sperm and calf thymus DNA renders this final argument moot.

In light of the above, Applicants respectfully submit that this rejection has been obviated by the above explanation and so may be properly withdrawn.

**Conclusion**

In light of the above amendments and arguments, Applicants respectfully submit that claims are in condition for allowance and respectfully urge early indication to this effect.

If the Examiner believes a telephone conference would expedite prosecution of this application, he is encouraged to telephone the undersigned at the number provided below.

Respectfully submitted,



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